10/092,549

C.A.S. 10.11.03

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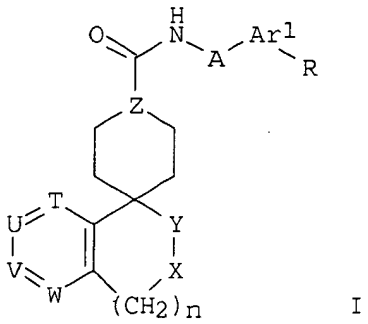
L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:133239 CAPLUS
DOCUMENT NUMBER: 138:170086
TITLE: Preparation of spiro[isoquinoline-piperidine], spiro[indoline-piperidine], and spirocyclohexane compounds as antagonists of neuropeptide Y receptor
INVENTOR(S): Fukami, Takehiro; Nonoshita, Katsumasa; Sagara, Takeshi; Kishino, Hiroyuki
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014083	A1	20030220	WO 2002-JP7922	20020802

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-239567 A 20010807
OTHER SOURCE(S): MARPAT 138:170086
GI



I

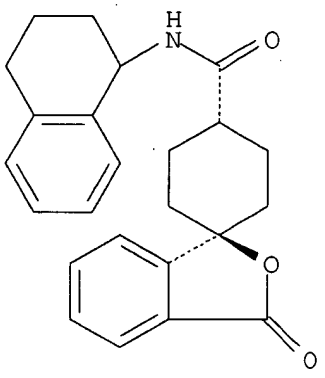
AB The invention relates to compds. such as spiro[cyclohexane-1,1'-(3'H)-isobenzofuran], spiro[4-, 5-, 6-, or 7-azaisobenzofuran-1(3H),1'-cyclohexane], spiro[indoline-3,1'-cyclohexane], spiro[indoline-3,4'-piperidine], spiro[isobenzofuran-1(3H),4'-piperidine], and spiro[isoquinoline-1(2H),4'-piperidine] represented by the general formula (I) or salts or esters thereof [A = linear C1-6 hydrocarbon group which may be substituted or interrupted by oxygen or nitrogen; Ar1 = (un)substituted aryl or heteroaryl; n = 0,1; R = H, lower alkylene; T, U, V, W = (un)substituted CH or N and at least 2 of T, U, V, and W is (un)substituted CH; X = -N(SO2R1)-, -N(COR2)-, or CO; Y = -C(R3)(R4)-, O, or -N(R5)-; and Z = CH or nitrogen; wherein R1 , R2, R5 = H, lower alkyl,

aralkyl, aryl; R3, R4 = H, HO, lower alkyl, aralkyl, aryl]. These compds. exhibit neuropeptide Y (NPY) receptor antagonism and are therefore useful as treating agents for various diseases in which NPY participates such as circulatory diseases, central nervous system diseases, and metabolic diseases, in particular over eating (hyperphagia), obesity, and diabetes. Thus, 64 mg 4-phenylcyclohexylamine hydrochloride and 115 mg 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride were added to a soln. of 74 mg trans-3'-oxospiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxylic acid in 2 mL pyridine and stirred at room temp. for 24 h to give trans-3'-oxo-N-(trans-4-phenylcyclohexyl)spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide (II). II and trans-N-[(S)-1-benzyl-2-(benzylamino)ethyl]-1-(methanesulfonyl)spiro[indoline-3,1'-cyclohexane]-4'-carboxamide showed IC50 of 2.5 and 0.69 nM for inhibiting the binding of [125I]peptide YY to human NPY Y5 receptor.

IT **497238-40-1P 497238-44-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiro[isoquinoline-piperidine], spiro[indoline-piperidine], and spiro[azaisobenzofuran-cyclohexane], and spirocyclohexane compds. as antagonists of neuropeptide Y receptor for treating overeating, obesity, and diabetes)

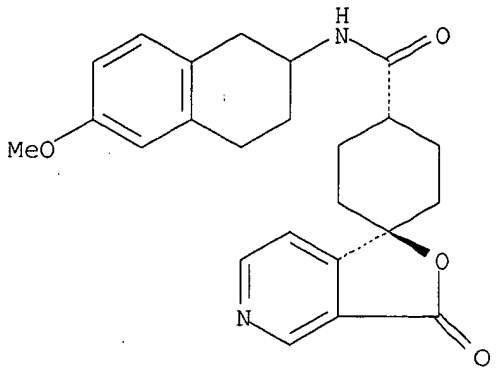
RN 497238-40-1 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide, 3'-oxo-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 497238-44-5 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-4-carboxamide, 3'-oxo-N-(1,2,3,4-tetrahydro-6-methoxy-2-naphthalenyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:97426 CAPLUS
DOCUMENT NUMBER: 138:137598
TITLE: Preparation of [11C]trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide (I) as radiolabeled neuropeptide Y Y5 receptor antagonist
INVENTOR(S): Burns, H. Donald; Gibson, Raymond E.; Hamill, Terence G.; Fukami, Takehiro
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003010175	A2	20030206	WO 2002-US23044	20020719

W: CA, JP, US
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

PRIORITY APPLN. INFO.: US 2001-307499P P 20010724

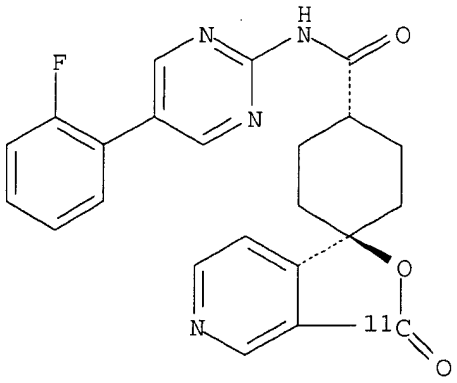
AB The present invention is directed to radiolabeled neuropeptide Y Y5 receptor antagonists, in particular [11C]trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide (I), which are useful for the labeling and diagnostic imaging of neuropeptide Y Y5 receptors in mammals (no data). Thus, a 1 mL vial was charged with 0.5 mg trans-4-(3-bromopyridin-4-yl)-4-hydroxy-N-[5-(2-fluorophenyl)-2-pyrimidinyl]cyclohexanecarboxamide and 1.2-1.4 mg Pd(PPh3)4 in 0.3 mL THF, capped, flushed with nitrogen, and shaken until homogeneous for 25 min at room temp. The mixt. was transferred with pressure (35 Mpa) to a microautoclave precharged with [11C]carbon monoxide and heated at 125.degree. and 5,000 psi for 5 min to give I.

IT **494802-27-6P**
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [11C]trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide as radiolabeled neuropeptide Y Y5 receptor antagonist for diagnostic imaging)

RN 494802-27-6 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-3'-11C-4-carboxamide,

N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:947029 CAPLUS
DOCUMENT NUMBER: 138:24705
TITLE: Preparation of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compounds as neuropeptide Y antagonists.
INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro
PATENT ASSIGNEE(S): Japan
SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Pat. Appl. 2002 52,371.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002188124	A1	20021212	US 2002-92549	20020308
JP 2003104884	A2	20030409	JP 2002-271261	20000817
US 6326375	B1	20011204	US 2000-640784	20000818
US 6335345	B1	20020101	US 2001-928431	20010814
US 2002052371	A1	20020502	US 2001-983598	20011025
US 6388077	B2	20020514		
US 6462053	B1	20021008	US 2002-101221	20020320
US 2002165391	A1	20021107		
US 2003055251	A1	20030320	US 2002-226225	20020823
WO 2003076443	A1	20030918	WO 2003-JP2611	20030305

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 1999-233573 A 19990820

JP 2000-137692 A 20000510
US 2000-640784 A3 20000818
US 2001-983598 A2 20011025
JP 2000-247145 A3 20000817
US 2002-92549 A 20020308
US 2002-101221 A3 20020320

OTHER SOURCE(S): MARPAT 138:24705

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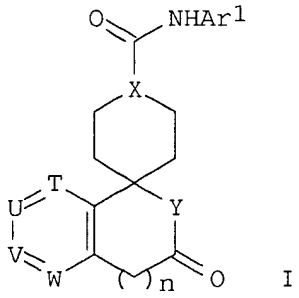


I

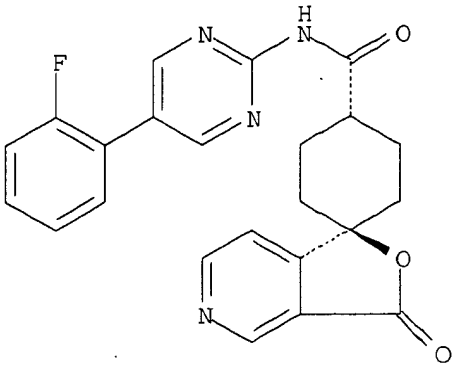
AB Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = CH, CH(OH); Y = (substituted) imino, O], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide (II), which inhibited [125I]neuropeptide Y binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

IT **328232-65-1P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

RN 328232-65-1 CAPLUS

CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-4-carboxamide, N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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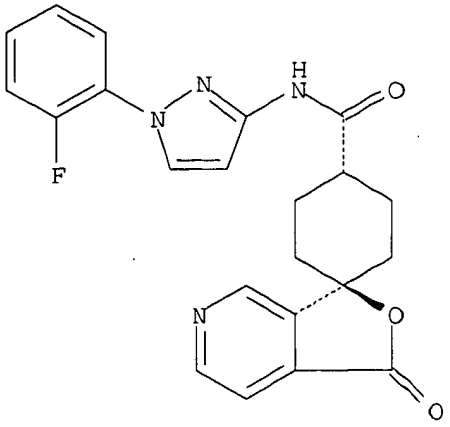
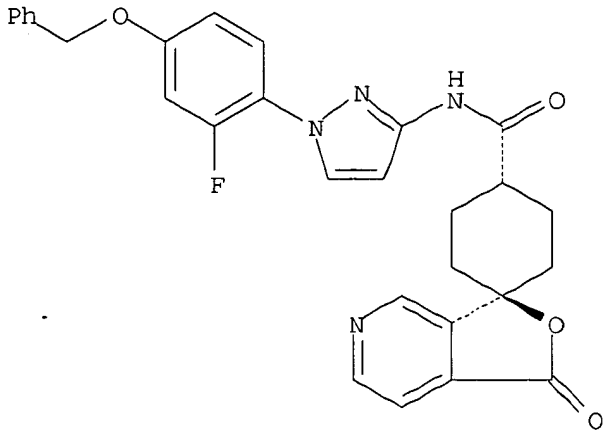


IT **478014-38-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)
RN 478014-38-9 CAPLUS
CN Spiro[cyclohexane-1,3'(1'H)-furo[3,4-c]pyridine]-4-carboxamide, N-[1-[2-fluoro-4-(phenylmethoxy)phenyl]-1H-pyrazol-3-yl]-1'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:152682 CAPLUS
DOCUMENT NUMBER: 134:207809
TITLE: Preparation of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compounds as neuropeptide Y antagonists.
INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 164 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014376	A1	20010301	WO 2000-JP5427	20000811
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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US 2003055251	A1	20030320	US 2002-226225	20020823

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JP 1999-233573 A 19990820
JP 2000-137692 A 20000510
WO 2000-JP5427 W 20000811
JP 2000-247145 A3 20000817
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US 2001-983598 A3 20011025
US 2002-101221 A3 20020320

OTHER SOURCE(S): MARPAT 134:207809
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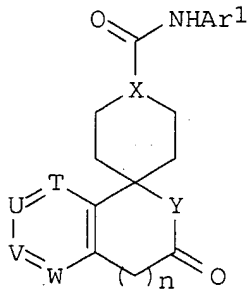

I

AB Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = N, CH; Y = (substituted) imino], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-

1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide, (II), which inhibited [125I]peptide YY binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

IT **328232-41-3P 328232-42-4P 328232-43-5P**
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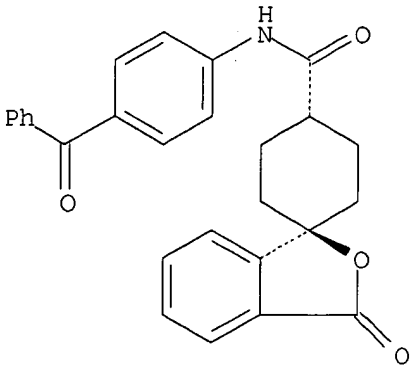
328232-95-7P 328232-96-8P 328232-97-9P
328232-98-0P 328232-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

RN 328232-41-3 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide, N-(4-benzoylphenyl)-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

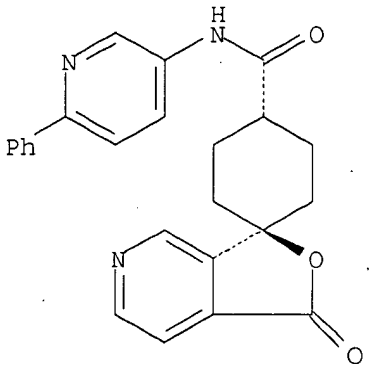


RN 328232-42-4 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide, 3'-oxo-N-(5-phenylpyrazinyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

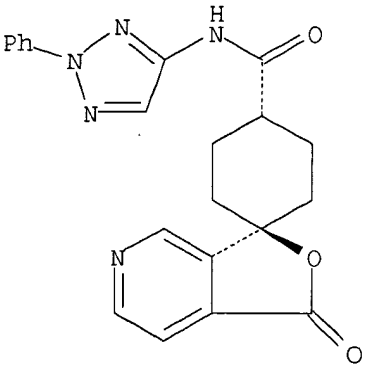
1'-oxo-N-(6-phenyl-3-pyridinyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



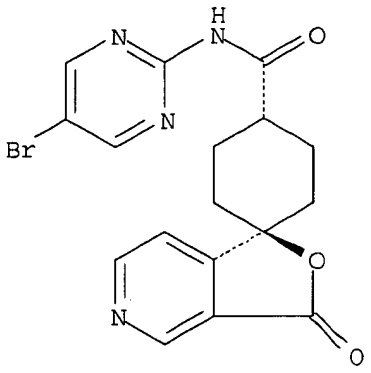
RN 328232-99-1 CAPLUS
CN Spiro[cyclohexane-1,3'(1'H)-furo[3,4-c]pyridine]-4-carboxamide, 1'-oxo-N-(2-phenyl-2H-1,2,3-triazol-4-yl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



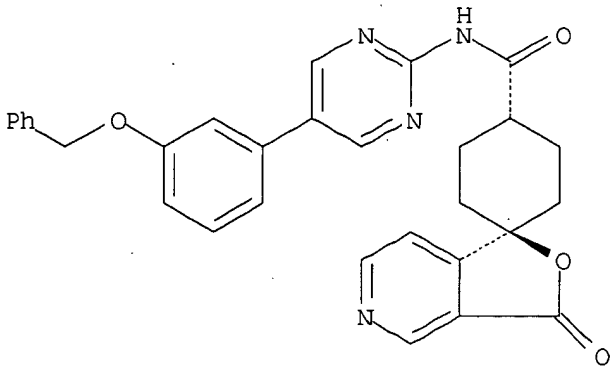
IT **328233-32-5P 328233-33-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)
RN 328233-32-5 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-4-carboxamide, N-(5-bromo-2-pyrimidinyl)-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 328233-33-6 CAPLUS
CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-4-carboxamide, 3'-oxo-N-[5-[3-(phenylmethoxy)phenyl]-2-pyrimidinyl]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

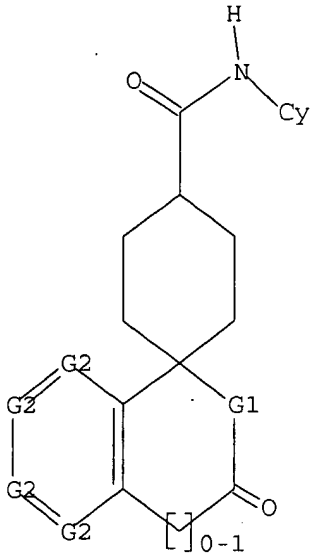
=> d his

(FILE 'HOME' ENTERED AT 14:35:33 ON 11 OCT 2003)

FILE 'REGISTRY' ENTERED AT 14:35:44 ON 11 OCT 2003
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 207 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:37:05 ON 11 OCT 2003
L4 4 S L3

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 O,N

G2 C,N

Structure attributes must be viewed using STN Express query preparation.